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SEMINAR ON COMPUTER APPLICATIONS FOR THE CARDIOLOGIST—V

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A Computer-Based Markov Decision Analysis of the Management of Symptomatic Bifascicular Block: The Threshold Probability for Pacing*

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This review illustrates the use of computer-based Markov models to estimate cost-effectiveness and prognosis in a complex problem in clinical cardiology.

Decision analysis and cost-effectiveness analysis were used to assess whether to implant a permanent cardiac pacemaker, treat with drugs, perform electrophysiologic studies or observe patients who have two clinical features—syncope and bifascicular block—that may or may not be causally related. Using a Markov process model, a computer program simulated the prognosis of five cohorts of such patients—one treated conservatively, one given empiric antiarrhythmic drug therapy, one receiving a pacemaker, one treated with empiric drugs and pacing and one tested with electrophysiologic studies. On the basis of data from published reports and expert opinion, quality-adjusted life expectancy was calculated by summing the average time a member of each cohort would survive with and without symptoms for each initial treatment choice. The costs were estimated from 1985 hospital charges.

For patients with normal left ventricular function, electrophysiologic testing provides a benefit of 14 quality-adjusted months of life over observation, at an additional cost of $24,200. Empiric pacing would add 2.5 additional months, at a further cost of $14,300. In patients with poor left ventricular function, empiric drug therapy offers 1.5 additional quality-adjusted months over observation, at a cost of $6,900. Electrophysiologic testing provides a further 16.5 months at an additional cost of $16,900. These results hold when the relation between symptoms and arrhythmia is not firmly established. Varying the probabilities of underlying ventricular tachyarrhythmias, bradyarrhythmic conduction defects or noncardiac causes of syncope affects the cost-effectiveness relative to the alternative treatments.

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Both medical (1–7) and lay publications (8–12) have suggested that physicians implant permanent transvenous cardiac pacemakers too often. The conclusions of the physician experts in these critical articles have been based on prospective and retrospective case by case analyses. These opinions have not, however, included a quantitative balancing of the costs and risks of not implanting a pacemaker, in patients whose symptoms could be alleviated and whose survival could be prolonged by such therapy, against the risks of implanting a pacemaker, in patients who really do not require one. This problem is well suited to clinical decision analysis (13–17) because the decision to employ a pacemaker should rest on a comparison of the benefits, risks and costs of a pacemaker with respect to the probability that pacemaker-responsive symptoms are present.

We addressed the specific question: in which patients with both syncope and bifascicular block should a pacemaker be inserted? Clearly, some patients have both findings: in some the symptoms are causally related to the conduction disturbance, and in others they are not. The risks of pacemaker therapy are low, but pacemakers are expensive. Nevertheless, patients with symptoms responsive to

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pacemaker implantation experience substantial gains in both survival and quality of life if a pacemaker is used (18). On the other hand, the omission of electrophysiologic testing may lead to inappropriate therapy in some patients with ventricular tachyarrhythmias. Thus, the quality-adjusted survival of some patients with symptoms causally related to arrhythmias will improve if their physicians implant a pacemaker before a relation between arrhythmia and symptoms is documented unequivocally, while other patients will be at additional risk for sudden death. In this study we analyze the benefits and risks of early pacemaker implantation in terms of quality-adjusted life expectancy and calculate the expected monetary costs of such therapy, compared with alternatives of empiric drug therapy and electrophysiologic diagnostic studies.

The data base on which physicians' decisions in this area rest is weak for several reasons. First, studies of the "natural history" of bifascicular block and other conduction disturbances often exclude patients with syncope and terminate follow-up when a pacemaker is implanted. Second, there has been no randomized controlled prospective trial of pacemaker therapy in such patients. Third, although bifascicular block can evolve into high degrees of atrioventricular (AV) block, patients with such advanced conduction disturbances are now uniformly treated by pacemaker implantation. Thus, contemporary natural history data in patients with high grade AV block are sparse.

Given current clinical practice, the data base describing the natural history of high grade conduction disturbances is unlikely to increase substantially, and our present study cannot improve that data base. Rather, we develop a prognostic model that utilizes the available data and shows under what range of assumptions the strategy of aggressive pacemaker implantation would be optimal.

Review of the Literature

In bifascicular block, as in any disorder of cardiac conduction, clinical concern centers around the possibility of cardiac slowing sufficient to cause syncope or sudden death. Prophylactic pacemaker insertion might prevent bradyarrhythmias, but it is costly and associated with some risk. The Framingham study (19) of 5,176 persons over age 18 years accumulated 125 cases of new left or right bundle branch block, or both, in 18 years, that is, 134 cases/100,000 patients per year. Thus, even if pacemaker insertion were risk free, the economic costs of prophylactic pacemaker insertion in all patients with newly acquired bundle branch block would be prohibitive. The current approach has been to identify patients with "high risk" conduction abnormalities (20). Little attention has been devoted, however, to defining the risk-benefit relation of early pacemaker implantation.

Risks of chronic bifascicular block. Although patients with chronic bifascicular heart block may develop AV block, this risk appears to be relatively low (19,21). Table 1 summarizes the results of two retrospective (22,23) and four prospective (24–26) studies involving 1,566 patients over an average of 2.9 years. Only 65 deaths possibly related to AV block (4.2%) were observed, although there was a 16.6% annual incidence rate of pacemaker insertion during the follow-up periods. The high prevalence of other cardiovascular diseases probably accounted for the high overall mortality (26). The rates of progression to complete heart block were also low, averaging 5% over the follow-up period. Some studies did not report symptoms, but those containing such data (23,24,26) included 85 patients, of whom roughly half had symptoms that could reasonably be attributed to AV block.

In patients with bifascicular block with prior syncope, however, the risk of progression to complete AV block is higher than in asymptomatic patients with bifascicular block. Of the 554 patients followed up by McAnulty et al. (26), a subgroup of 47 persons had syncope at some time before entry into the study and 8 had syncope at the time of entry into the study. The syncope was determined to be secondary to heart block in none of these 55 individuals. During a mean follow-up period of 42.4 months there was a 17% incidence rate of heart block in individuals with syncope, compared with a 2% incidence rate in those without syncope

Table 1. Reported Prognosis of Chronic Bifascicular Heart Block

Study	No. of Patients	Follow Up (yr)	Dead	Death Possibly Caused by AV Block	Symptoms Probably Caused by Bradyarrhythmia	Symptoms Probably Not Caused by Bradyarrhythmia	Paced	AV Block
Scanlon (22)	209	2	31	3(1.4%)				30(14.4%)
DePasquale (23)	83	3.1	19	1(1.2%)	5(6.0%)	3(3.6%)	5	2(2.5%)
Narula (24)	83	3	32	1(1.2%)	19(22.9%)	11(13.6%)	28	4(4.8%)
Dhingra (25)	531	3.3	207	42(7.9%)			32	21(4.0%)
Kulbertus (25a)	106	3	10	0				2(1.9%)
McAnulty (26)	554	3.5	160	18(3.2%)	19(3.4%)	28(5.0%)	30	19(3.4%)
Total	1,566	2.9	459	65(4.2%)	43(6.0%) of 720	42(5.8%) of 720	95 of 752	78(5.0%)

($p < 0.05$). Additionally, sinoatrial disorders occurred in 18% of the patients with syncope. Like patients with AV block, individuals with sinus node dysfunction would have pacemaker-responsive symptoms but would not experience prolonged survival.

In the subsequent analysis we shall assume that patients with bifascicular block who develop high grade AV block become subject to the same risks as patients who initially present with AV block. Thus, the risks of high grade AV block are considered next.

Risks of high grade AV block. Permanent ventricular pacing has been the treatment of choice for high grade AV block for 20 years; pacing has prolonged the life of patients with this disorder. If underlying cardiovascular disease is present, the expected survival of these patients, even with permanent pacing, is less than that of members of the general population of the same age (27,28). Table 2 summarizes the survival of 178 untreated patients (29,30) and 1,268 patients treated with pacemaker implantation (27–33). The limited availability of data describing the natural history of high grade AV block reflects the worldwide acceptance of pacemaker implantation as therapy for that entity. The 2 year survival rate for unpaced patients was 45.5% compared with 78.3% for patients treated with a pacemaker. The mortality rate in these patients was related to underlying cardiovascular disease, decreased cardiac output or congestive heart failure and advanced age (Table 3) (28,30,31,33,34).

In a series composed largely, although not entirely, of patients with AV block, Furman (35) reported the long-term survival of 1,500 patients receiving a pacemaker. The 2 year survival was 80%, survival at 5 years was 65% and survival at 10 years was 40%. He suggested that these results were comparable with those for members of the general population of the same age and sex.

Thus, chronic bifascicular heart block has a relatively good prognosis but can evolve into complete heart block, a disorder with poor prognosis unless a pacemaker is inserted. Investigators have therefore examined techniques for identifying patients at high risk for developing complete heart block.

Predictive value of electrophysiologic testing. At present, detailed recommendations regarding the role of invasive electrophysiologic studies and evaluation of patients with bifascicular block and syncope are difficult to formulate, in part because of the limitations inherent in published data derived from highly selected patient populations and to variation in testing protocols (36–42). However, two recently published studies (43,44) provide data that impact on the role of electrophysiologic testing in the evaluation of patients with syncope and bifascicular block. Ezri et al. (43) studied 13 patients using programmed ventricular stimulation (six had coronary artery disease, three had cardiomyopathy and four had no evidence of organic heart disease). Holter monitoring and neurologic evaluation were nondiagnostic in all patients prior to electrophysiologic testing. The results of the studies included inducible ventricular

Table 2. Reported Prognosis of High Grade AV Block

	Unpaced		Paced	
Study	No. of Patients	Survival	No. of Patients	Survival
Johansson (30)	119	50% (1 yr) 44% (2 yr)	101	87% (1 yr)
Mascarenhas (31)			230	79.6% (1 yr) 72.2% (2 yr)
Amikam (32)			80	90% (1 yr) 82.1% (2 yr) 58.3% (5 yr)
Rettig (27)			369	79.9% (2 yr) 65.6% (4 yr) 53.7% (6 yr)
Ohm (29)	59	63% (1 yr) 47% (2 yr)	122	87% (1 yr) 83% (2 yr)
Simon (28)			246	88% (1 yr) 61% (5 yr) 49% (10 yr)
Alpert (33)			120	91% (1 yr) 63% (5 yr) 49% (10 yr)
Total	178	56.5% (1 yr) 45.5% (2 yr)	1268	85.9% (1 yr) 78.3% (2 yr) 59.4% (5 yr) 46.4% (10 yr)

Table 3. Reported Relation of Underlying Disease to Survival in Pacemaker Treated High Grade AV Block

Study	Underlying Disease	No. of Patients	Survival (%)			
			1 Yr	2 Yr	5 Yr	10 Yr
Mascarenhas (31)	Stokes-Adams alone	48	91.7	85.4		
	Stokes-Adams with decreased cardiac output or congestive heart failure	118	83.9	77.9		
	No Stokes-Adams but complete heart block with congestive heart failure	64	62.5	50		
Simon (28)	Congestive heart failure	89	85	75	55	
	No congestive heart failure	157	90	85	69	
	Idiopathic	113		87	72	
	Ischemic/hypertensive	67		65	40	
	Age < 65	86			75	
	Age 65 to 74	93			61	
	Age ≥ 75	67			40	
Alpert (33)	Conduction system disease only	46	92		79	68
	Congestive heart failure	48	87		49	19
	Age < 66	33	90		65	42
	Age 66 to 74	34	87		64	43
	Age ≥ 75	53	95		61	38
	Coronary heart disease	35	89		51	28
	Diabetes	29	97		68	41
	Hypertension	14	89		63	35
	Valvular heart disease	11	78		63	53

tachycardia in four patients, an HV interval greater than 70 ms in four, and intraHis and infraHis bundle block with atrial pacing in one, and were nondiagnostic in four patients. Four of the five patients with a prolonged HV interval or pacing-induced infranodal block and one with a nondiagnostic study received a permanent pacemaker. The four patients with ventricular tachycardia received antiarrhythmic therapy, and three of the four patients with nondiagnostic studies received no therapy. During a mean follow-up period of 9 months, all but three patients had been free of syncope. One patient did not take prescribed antiarrhythmic therapy, another patient with ventricular tachycardia died suddenly and the remaining patient had a normal study and was eventually shown to have basilar migraines.

In a similar study, Morady et al. (44) identified abnormal infranodal conduction times in 12 (38%) of 32 patients and found pathologic infranodal block during atrial pacing in 2 (6%). Unimorphic ventricular tachycardia was induced in nine patients (28%) and polymorphic ventricular tachycardia in five (16%). In general, a permanent pacemaker was implanted in patients with infranodal block or a prolonged HV interval. Patients with ventricular tachycardia were treated with an antiarrhythmic drug. The mean follow-up period was 19 months. There were three sudden deaths: in a noncompliant patient with inducible sustained ventricular tachycardia; in a patient treated empirically with quinidine for premature ventricular complexes and in a patient with a prolonged HV interval treated with a permanent pacemaker. The actuarial incidence of sudden death was 10% at 45 months of follow-up. Only two patients had recurrent syncope; both had a normal electrophysiologic study. Thus, approximately 50% of patients with bundle branch block and unexplained syncope who underwent electrophysiologic testing were found to have at least one clinically significant abnormality.

Although prospective, randomized therapy has not been reported, approximately 85% of patients whose treatment was based on the results of electrophysiologic testing did not experience recurrent syncope. In 204 patients with syncope not selected for bifascicular disease, Kapoor et al. (45) identified a cardiovascular cause in 53 and a noncardiac cause in 54. Of the 23 patients who underwent electrophysiologic testing, 3 were found to have inducible ventricular tachycardia not documented by electrocardiographic monitoring, 2 had a prolonged HV interval, 1 patient with clinical evidence of sick sinus syndrome had a prolonged sinus node recovery time, 2 patients had inducible supraventricular tachycardia, 3 had a nondiagnostic prolonged effective refractory period of the AV node and 12 patients had a nondiagnostic study. The therapy that was instituted was based on these findings. After 1 year, the overall mortality rate was 30% in patients with a cardiovascular cause (24% incidence of sudden death), 12% in patients with established noncardiac causes (4% incidence of sudden death) and 6.4% in patients with syncope of unknown origin (3% incidence of sudden death).

Although three prospective studies have failed to demonstrate a consistent relation between progression of infranodal conduction system disease and electrophysiologic testing results (26,46,47), the patient populations and the

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study protocols were markedly different from those used by Ezri and Morady and their colleagues (43,44). McAnulty et al. (26) identified patients with conduction system disease based on screening electrocardiograms. Any patient with symptoms documented to be due to bradyarrhythmia was excluded and treated with a pacemaker. Similarly, Dhingra et al. (46) found that 38% of 452 asymptomatic patients with chronic conduction system disease had evidence of impaired infranodal conduction. Peters et al. (47) analyzed the clinical and serial electrophysiologic variables associated with progressive disease in 90 patients undergoing at least two electrophysiologic studies. Neither age, cardiac diagnosis, New York Heart Association classification, electrocardiographic patterns, nor initial abnormal infranodal conduction was a reliable marker for progression.

By contrast, Scheinman et al. (48) found a greater rate of progression to second or third degree AV block in patients with impaired infranodal conduction. Of 121 patients followed up for a mean of 18 months, 21% with abnormal infranodal conduction progressed to second or third degree AV block as compared to 1.3% with normal infranodal conduction.

In this review we will build an analytic computer model of the decision to pace or treat empirically, to conduct electrophysiologic testing or to observe a patient with chronic bifascicular heart block and unexplained syncope, and will compare the costs and medical effects of each proposed strategy.

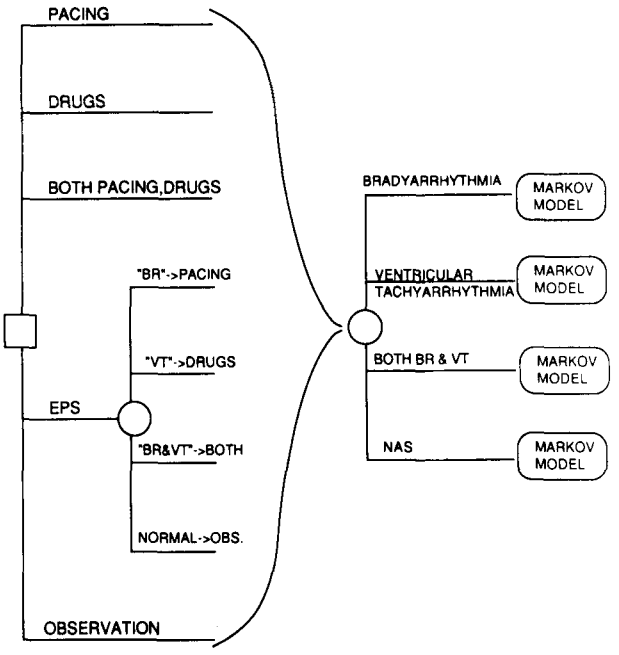

Figure 1. Decision tree. Five strategies are proposed for the management of symptomatic bifascicular block. Empiric pacing, antiarrhythmic drugs, both pacing and drugs and observation (OBS.) lead to the distal chance node (**circle**) at right. Electrophysiologic testing (**EPS**) leads to a first chance node (**circle**) at which the appearance at electrophysiologic testing and the consequent management plans are described. BR = bradyarrhythmia; NAS = nonarrhythmic syncope; VT = ventricular tachyarrhythmia.

Methods

The problem. Consider a patient who presents with repeated syncopal episodes without a clear precipitating cause. The routine electrocardiogram demonstrates bifascicular block. Ambulatory electrocardiographic monitoring fails to demonstrate either AV block or bradycardia, but no syncopal episodes occurred during the 24 hour recording. (We exclude patients who develop documented AV block or bradycardia with syncope because they will surely receive a pacemaker. We also exclude patients who develop their typical syncope without documented arrhythmia because in such cases the findings are most likely unrelated.) Should a permanent pacemaker be implanted? Should electrophysiologic testing be performed? In this analysis we will consider patients who have normal ventricular function separately from those who have serious left ventricular disease, because the spectrum and risks of arrhythmias differ.

Therapeutic approach. Five alternative strategies are proposed for the problem of unexplained syncope in bilateral bundle branch block (Fig. 1, left). 1) A patient may be prophylactically paced, effectively abolishing the chance of progressive heart block. 2) To treat possible ventricular tachyarrhythmias, he or she may be given a trial of antiarrhythmic agents. 3) These therapies can be combined. 4) A patient may be submitted to electrophysiologic testing, or 5) observed for progression of arrhythmia. For any one of these strategies, the patients may have one of four possible causes of syncope (Fig. 1; right): bradycardic conduction defects, ventricular tachyarrhythmia, both causes, or nonarrhythmic syncope.

If the decision is made to conduct electrophysiologic testing, however, four results are possible: 1) A bradyarrhythmia (conduction delay) or block will be detected, leading to pacemaker implantation; 2) a ventricular tachyarrhythmia will be detected, leading to a trial of medication, repeat studies and follow-up; 3) both conduction disease and ventricular tachyarrhythmias will be identified, leading to both types of treatment; or 4) electrophysiologic testing will be normal. In the last event, we assume the diagnosis of nonarrhythmic syncope will be made and the patient will be treated conservatively (44). Of course, the electrophysiologic testing result will not always be correct; a proportion of patients with each type of syncope will be falsely classified; thus, the results of electrophysiologic testing are shown in quotes in Figure 1.

Table 4 contains the data used in the decision tree, subjectively obtained from an experienced clinical electrophysiologist. In patients with normal left ventricular function, bradyarrhythmic conduction disturbances and noncardiac

Table 4. Assumptions About Causes of Syncope and Appearance at Electrophysiologic Testing

Etiology	Prevalence (fraction of cohort)		Appearance at Electrophysiologic Testing			
			BR	VT	Both	NAS
A. Left Ventricular Ejection Fraction Normal						
BR	0.50	—	0.60	0.10	0.05	0.25
VT	0.10	—	0.25	0.55	0.10	0.10
Both	0.05	—	0.20	0.20	0.30	0.30
NAS	0.35	—	0.20	0.05	0.05	0.70
B. Left Ventricular Ejection Fraction <40%; Coronary Disease With Prior MI						
BR	0.25	—	0.40	0.15	0.20	0.25
VT	0.45	—	0.05	0.65	0.25	0.05
Both	0.10	—	0.05	0.35	0.55	0.05
NAS	0.20	—	0.10	0.20	0.05	0.65

Both = both ventricular tachyarrhythmia and bradyarrhythmia; BR = bradyarrhythmia/conduction disturbance; MI = myocardial infarction; NAS = nonarrhythmic syncope; VT = ventricular tachyarrhythmia.

syncope are the most common etiology, occurring in 50% and 35%, respectively, of a cohort of patients with chronic bifascicular heart block and syncope. Electrophysiologic testing identifies bradyarrhythmic lesions, ventricular tachyarrhythmias and nonarrhythmic syncope in more than half of the cases. In patients with poor left ventricular function and a cardiac history, ventricular tachyarrhythmia is the etiology in almost half of the patients; in these, therefore, electrophysiologic testing would be most sensitive to ventricular tachyarrhythmias and combined etiologies. Under all scenarios, the natural history of the patient's arrhythmia, underlying cardiovascular disorders and co-morbidity must be modeled. We model cardiac and noncardiac mortality separately. We also keep a separate record of the frequency and consequences of AV block.

Markov model. We will simulate the prognosis of not one, but 1 million patients with the same findings. We simulated the natural history of this cohort of patients, using a well established decision theoretic approach—the Markov process assumption (49). In this model, we assumed that a patient's current age and state of health predict the future behavior of a cohort of similar patients (50). We calculated the number of patients in each state and the number of transitions among states that would be expected to occur each month.

Using the Markov model, we performed separate computer simulations for each disease and initial treatment option. For treatments not involving initial pacemaker implantation (with or without antiarrhythmic drugs), we began with a cohort of 1 million patients initially in a state labeled "no AV block"; we assumed that the cohort would be followed up for the development of AV block. When AV block develops, a pacemaker would be implanted. For treatment involving initial pacemaker implantation (with or without drugs), we assumed that the cohort would be followed up for the development of pacemaker failure. We continued each simulation until all members of each cohort were in the state "dead." Probabilities of sudden cardiac death depended on the underlying cause (that is, tachycardia, bradycardia, both, and nonarrhythmic syncope) and the treatment (pacing, drugs, both, neither). The total number of months of survival, with appropriate quality adjustments (see later), was calculated for each cohort. Those totals, divided by the initial cohort size, were used as an approximation of the "quality-adjusted life expectancy."

At any given moment, each patient is in one of three major states (Fig. 2): 1) not having AV block, 2) having AV block, or 3) dead. The likelihood of transition between one state and another depends on well defined probabilities. A patient without AV block may be "unpaced" or "paced"; that is, a permanent cardiac pacemaker may already have been implanted. The patient with a pacemaker is subject to complications, generator changes and sudden pacemaker failure. In those patients who have symptoms related to bradycardia, pacemaker implantation provides symptomatic improvement and prevents asystole if AV block develops. If the heart is not paced, sudden death can occur when AV block develops. We assume that a pacemaker will be implanted when AV block is diagnosed if the heart is unpaced at that time. Finally, a patient may die from several causes: 1) bradyarrhythmia, 2) ventricular tachyarrhythmia, 3) the general spectrum of other risks faced by healthy members of the general population of the patient's age and sex, or 4) some other disease process, cardiac or noncardiac, for example, diabetes or cancer. The "temporary states" represented by shaded circles in Figure 2 (acute AV block, pacemaker implantation, generator changes and pacemaker failures) were assumed to last only a single month.

We did not use a first order Markov model in this case, that is, the probability of death in the general population was modeled to increase exponentially with age. Although bifascicular block can be progressive, the available reported

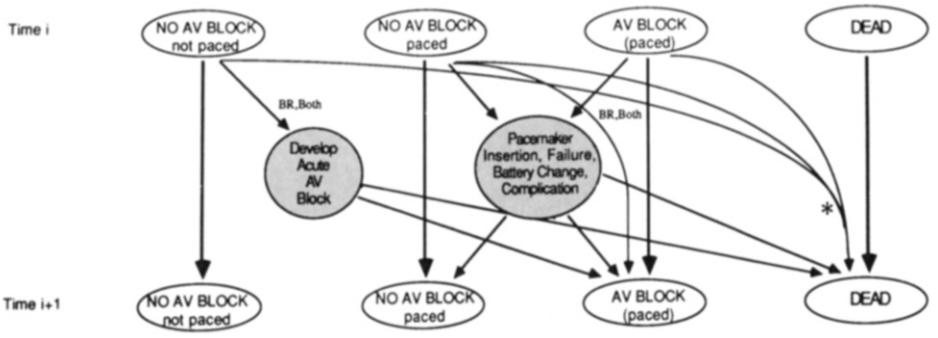

Figure 2. Markov model. Four major clinical states are depicted: no AV block not paced, no AV block paced, AV block, and dead. At **Time i** a cohort member is in one of these states of health. At **Time i+1** the patient has either remained in the starting state (**heavy vertical arrows**) or changed to another major state. The patient with no AV block can remain in that status, develop acute AV block if the heart is not paced (**shaded oval**), transit to stable AV block if empiric pacing is instituted, or die as a result of a number of causes. All patients with stable AV block will have pacing. The **shaded ovals** represent temporary events associated with a short-term decrement in quality of life and an increased risk of death: 1) acute AV block as described, and 2) pacemaker events and complications. The **asterisk** (*) signifies death due to underlying disease, cardiac arrhythmia other than AV block, or general population (Gompertz) mortality. Abbreviations as in Figure 1.

data (Tables 1 and 2) do not support a specific model of progression. We therefore chose to use a constant, average transition probability from bifascicular to AV block. AV block itself confers a constant added risk of death on a patient.

Variables of the Markov model (Table 5). We relied heavily on the report by McAnulty et al. (26) for natural history, and on expert opinion for the distribution of cause of syncope and risks of sudden death. Of patients with chronic bifascicular heart block and symptoms related to bradyarrhythmias, 20% will develop AV block within 5 years and will be subject to a 10% risk of dying before a pacemaker can be implanted. With AV block, the excess

Table 5. Markov Transition Probabilities

From	To	Transitions/1,000 Patient Months
Chronic bifascicular block (syncope)	AV block	3.7
Chronic bifascicular block (syncope)	Bradyarrhythmic	1.0
AV block	Cardiac death	7.6
Pacemaker	Pacemaker failure	10
General population	Death (all causes)*	Age 65: 2.3
		Age 70: 3.6
		Age 75: 5.6
Underlying illness	Death due to that illness	0**

		Therapy	Poor Left Ventricular Ejection Fraction	Normal Left Ventricular Ejection Fraction
Bradyarrhythmia/conduction disturbance	Cardiac death	No pacing	12.5	8.3
		Pacing	8.3	4.2
Ventricular tachyarrhythmia	Cardiac death	No drugs	25.0	16.7
		Drugs	20.8	12.5
		Electrophysiologic testing and drugs	8.3	4.2
Both	Cardiac death	No pacing or electrophysiologic testing	25.0	16.7
		Pacing	20.8	12.5
		Electrophysiologic testing and drugs	16.7	12.5
		Electrophysiologic testing, drugs, pacing	8.3	8.3
Nonarrhythmic syncope	Cardiac death	All therapies	4.2	0

*Gompertz model: $1 - \exp[-7.3 \times 10^{-5} \times \exp(8.05 \times 10^{-2}\ \text{age})]$. **Baseline load.

mortality is 9.1%/year (or 7.6 deaths/1,000 patient months). We assumed that the annual risk of dying from "general causes" increases exponentially with age, roughly doubling every 8 years, as it does in the general population (following Gompertz's law (51,52). We used reported mortality data for the United States (53) to derive the regression coefficients for the Gompertz equation.

In assessing the incidence of pacemaker complications, we deliberately chose high values to bias the analysis against aggressive implantation. We assumed that 1) pacemaker insertion complications result in a 0.1% mortality rate, 2) the battery life of current lithium units is 6 years, and 3) unscheduled pacemaker failure occurs in 1% of units over their effective lifetime. At the time of pacemaker failure, we assumed a 20% risk of dying if AV block was present because the patient's intrinsic pacemaker activity would have been suppressed.

The risk of sudden death under the various syncopal etiologies and treatment plans in Table 5 was estimated by an expert electrophysiologist and also represents the expected number of deaths per 1,000 patient months.

Those patients whose symptoms are not pacemaker responsive were assumed to have some illness that did not diminish their life expectancy beyond the effects of their underlying cardiac disease, as manifested by the bifascicular block. This assumption does not introduce any bias into either the threshold or cost-effectiveness calculations (see later).

Threshold model. In this analysis, we are investigating the rationale for implanting a pacemaker or performing electrophysiologic testing in symptomatic patients *without documented AV block.* Thus, pacemaker implantation may or may not be effective in any individual patient. Since this probability is of great importance, we repeated our analysis for a broad spectrum of probabilities of bradyarrhythmia and ventricular tachyarrhythmia. The probability of pacemaker-responsive symptoms above which aggressive therapy is preferable is called the threshold probability (15) for pacing.

Concept of "load." Patients with syncope related to a bradyarrhythmia sometimes have no underlying cardiac or other serious disease. In that situation, their only risk of death, over and above those facing the general population, is related to bradyarrhythmias. More commonly, these patients have underlying cardiovascular disease. Then, the potential benefits of pacemaker therapy are limited by these other processes; that is, pacemaker therapy cannot diminish these additional risks. In fact, risks not responsive to pacemaker therapy are not limited to cardiovascular disease; the effects of cancer would be analogous. The term "load" describes these noncorrectable risks. Obviously, the higher the load, the shorter will be the patient's survival. Thus, the efficacy or benefit of pacing, as measured by prolonged survival, will be diminished if the load increases. In patients with ventricular tachyarrhythmias, in addition to bradyarrhythmia, sudden death is an additional "load," but one accounted for explicitly in the model.

Table 6. Quality of Life With Various Therapies

Therapy	Clinical Status	Quality of Life (% month)
Pacemaker	No syncope	100
Drugs	No syncope	95
Both pacemaker and drugs	No syncope	90
No therapy	Syncope	75
Pacemaker	Syncope	70
Drugs	Syncope	65
Both pacemaker and drugs	Syncope	60
Hospitalization for any reason		50

Effects on quality of life. Pacemaker therapy improves a patient's quality of life when it relieves symptoms (that is, syncope) or lessens anxiety by providing "insurance" against life-threatening bradycardia. It can diminish a patient's quality of life by creating concern about being dependent on a pacemaker and the potential for that device failing (54) and by necessitating the inconvenience of ongoing follow-up and monitoring. We diminished the quality of life of a patient who continues to experience syncope; each month with syncope was counted as only a fraction of a "well" month. For example, if syncope diminished quality of life by 25%, then each month of survival with continued symptoms was adjusted for this quality and counted as 3 weeks of survival. Approximately 20% of patients receiving antiarrhythmic drugs experience substantial side effects that reduce their quality of life by approximately the same amount as patients having recurrent syncope, so a 5% overall quality of life adjustment was made for antiarrhythmic therapy. In the same fashion, whenever the patient had a pacemaker implantation or course of drug therapy, the quality of life for all subsequent months was slightly diminished to reflect anxiety and the necessity for follow-up. For example, if drug therapy diminished quality of life by 5%, then each year of survival with therapy was counted as only 49.4 quality-adjusted weeks. If the patient was unfortunate enough to continue to have syncope after antiarrhythmic therapy, then the quality of life was diminished by both factors. For example, if the mentioned factors of 25 and 5%, respectively, were both operative, then quality would be adjusted to 75% × 95% or roughly 70% of full quality: each year would count as only 36 quality-adjusted weeks. Pacemaker complications, pacemaker failure and routine battery changes were assumed to diminish the quality of life only for the month in which the complication or hospitalization occurred.

We administered a questionnaire to 16 cardiologists attending a pacemaker conference and assigned baseline values for the defined quality-adjustment factors based on their

responses. Collectively, these physicians treat more than 4,000 patients with a permanent cardiac pacemaker. They were asked to report their perceptions of the loss of quality of life that their patients experience as consequences of pacemaker therapy. Their assessments of the quality of life in various clinical states are summarized in Table 6.

Costs. We based our estimates of medical costs on 1985 charges at a teaching hospital. Pacemaker implantation cost $15,370 (that is, hardware $4,100, professional fees $1,880, and hospital charges $9,390 for a 6 day admission). Generator changes cost $11,130 (that is, hardware $2,000, professional fees $970 and hospital charges $8,160 for a 5 day admission). Charges for replacement were less, on average, because some companies provide replacement units free as a part of their warranty policy and because the electrode is not usually replaced.

Average electrophysiologic testing charges depended on the results of the study. If a pacemaker-responsive lesion was discovered, a pacemaker was implanted at the time of testing, yielding hospital charges of $11,800 and professional fees of $3,080 for an 8 day admission, plus the pacemaker cost of $4,100, for a total of $18,980. If ventricular tachyarrhythmia was discovered, the cost totaled $14,140 (that is, $10,990 for two studies and professional fees of $3,150, over a 9 day admission). If the study was nondiagnostic, the charges were $4,980 (hospital charges totaled $3,660 and professional fees $1,320 for a 3 day admission). Outpatient visits every 4 months cost $75, including the cost of an electrocardiogram. Monthly transtelephonic monitoring cost $45. Drug therapy for ventricular arrhythmias (procainamide and tocainide) cost $140/month.

Discounting. Future costs were discounted at 5%/year to reflect the fact that if an expense can be deferred, the requisite resources can be invested to yield returns before the costs are incurred. Future years of life (that is, benefits) were also discounted to maintain internal consistency in our analysis (55). The discounting of future benefits reflects both risk aversion (56) and the decreasing marginal value of life associated with aging.

Marginal cost-effectiveness. The conservative strategy of implanting a pacemaker only when AV block is documented should prevent subsequent bradyarrhythmic events. The aggressive strategy of implanting a pacemaker before AV block is documented or giving empiric drug therapy, or both, might provide some additional (or marginal) survival at some additional (or marginal) cost. These additional costs are incurred because the pacemaker would be implanted sooner in patients who eventually develop AV block and in some patients who would never develop AV block and would not receive a pacemaker under the conservative strategy.

Results

Expected costs, survival and quality of life. Although many analyses were performed in this study, only a selection will be reported here. We consider the case of a 65 year old man with syncope of unknown origin. Table 7 displays the results using baseline data, in the settings of 1) normal left ventricular function and 2) decreased left ventricular ejection fraction in the setting of coronary artery disease.

The patient with normal left ventricular function is most

Table 7. Baseline Results: 65 Year Old Man

Strategy	Costs ($)	Expected Survival (Mo)	Quality-Adjusted Survival (Mo)	Marginal Cost* ($)	Marginal Quality-Adjusted Survival*	Marginal Cost-Effectiveness*† ($/Year)
Normal Left Ventricular Function						
Observation	3,260	116.6	60.1	—	—	—
Drugs	14,800	117.8	54.9	11,540	−5.2	—
Electrophysiologic testing	27,450	134.4	73.8	24,190	13.7	21,200
Pacing	41,710	137.1	76.3	14,260	2.5	68,400
Both pacing and drugs	55,760	138.3	70.9	14,050	−5.4	—
Poor Left Ventricular Function						
Observation	1,360	61.4	35.8	—	—	—
Drugs	8,290	64.1	37.3	6,930	1.5	55,400
Electrophysiologic testing	25,190	85.2	53.8	16,900	16.5	12,300
Pacing	26,730	67.8	40.6	1,540	−13.2	—
Both pacing and drugs	34,930	70.5	42.7	9,740	−11.1	—

*Compared with prior nondominated strategy (see text for details). †Final column is calculated by dividing column 5 by column 6 and multiplying by 12.

likely to have a bradyarrhythmia or conduction defect (Table 4). Empiric treatment with both antiarrhythmic agents and a pacemaker provides the greatest survival (138 months), at a discounted cost of nearly $56,000. Empiric pacing offers nearly the same survival at substantially less cost ($42,000). A diagnostic approach using electrophysiologic testing offers a slightly lower survival rate, at even less cost. Empiric drug therapy and observation are associated with substantially less expected survival. When the quality of a patient's life is considered, rather than the expected survival, the effectiveness of therapy is decreased. In this case, the expected utility of empiric drug therapy falls below that of observation, while empiric combined therapy falls below empiric pacing and electrophysiologic testing (Fig. 3A).

In the setting of poor ventricular function and a history of coronary artery disease, ventricular tachyarrhythmia is the most likely cause, while bradyarrhythmic conduction disturbances alone comprise only 25% of causes (Table 4). Because of the increased probability of ventricular arrhythmias, electrophysiologic testing offers the greatest survival time in this type of patient (Table 7). Costs are less than in patients with normal left ventricular function, because survival time is shorter. Empiric therapy with both antiarrhythmic agents and pacing is again the most expensive. Adjusting for quality of life does not change the ordering of strategies (Fig. 3B).

Marginal cost/effectiveness ratio. Because we live in a world of limited resources, it is not always possible to provide every patient with the medical therapy that maximizes his or her individual survival. In choosing among feasible alternatives the physician and the health policy analyst should consider some metric that compares the relative cost and effectiveness of competing strategies. One appropriate metric is the marginal cost/effectiveness ratio which, in this case, expresses how much additional survival can be "bought" for each additional dollar expended. (If one strategy costs more than another strategy and provides less effectiveness, then the more costly strategy is said to be dominated and can be rejected from further consideration.)

Table 7 lists the marginal cost-effectiveness of each strategy, that is, the difference in its quality-adjusted survival and that of the next cheapest strategy. In the patient with normal left ventricular function, pacing offers 2.5 additional quality-adjusted months of survival compared with electrophysiologic testing. If any strategy provides a negative marginal effectiveness (for example, "drugs" and "both pacing and drugs"), it is dominated and rejected. Thus, the marginal effectiveness of electrophysiologic testing is 13.7 months because it is compared with observation and not empiric drug therapy, which has been rejected. In considering the marginal cost of each plausible strategy, empiric drug therapy and empiric dual therapy are again rejected because they are dominated. Thus, the marginal cost of electrophysiologic testing is $24,190 ($27,450 minus $3,260). From

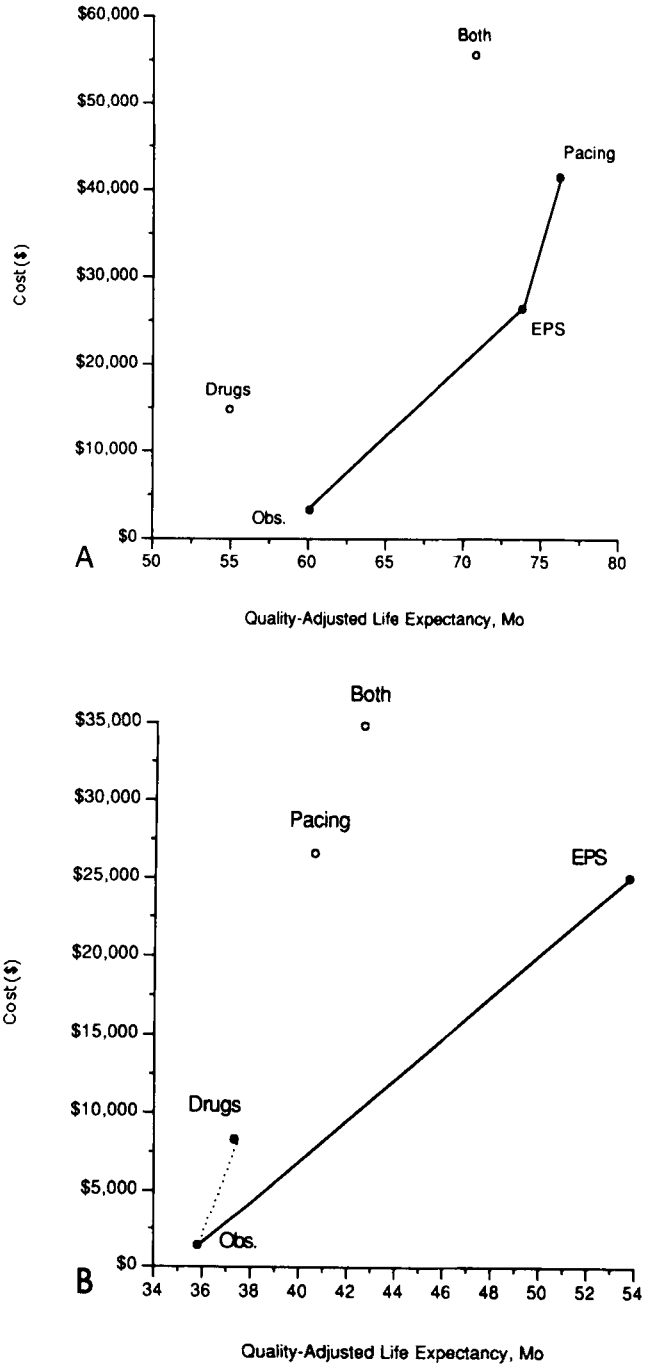

Figure 3. Cost-effectiveness plot. The **closed points** represent plausible strategies, the **open points** dominated strategies. **A,** Patient with *normal left ventricular function.* The plausible strategies, in order of cost and effectiveness, are observation (Obs.), electrophysiologic testing (EPS), and pacing, connected by a **solid line. B,** Patient with *poor left ventricular function.* The effective strategies are observation, drugs and electrophysiologic testing. However, the marginal cost-effectiveness of drugs with respect to observation is higher (**dotted line**) than that of electrophysiologic testing versus observation (**solid line**). Thus, electrophysiologic testing is more cost-effective than drug therapy (see text for details). The marginal cost/effectiveness ratio refers to the slope of lines connecting plausible points; the lower the slope, the more cost-effective the strategy.

the ratio between marginal cost and marginal effectiveness, we can express the results as additional dollars per additional life-year saved. The three plausible strategies for a man with normal left ventricular function are observation, electrophysiologic testing and empiric pacing. The marginal cost/effectiveness ratio of electrophysiologic testing is $21,200/additional quality-adjusted life-year gained; the marginal cost/effectiveness ratio of empiric pacing is $68,400/quality-adjusted year.

In the patient with poor left ventricular function (Table 7), the plausible strategies are observation, empiric drug therapy ($55,400/quality-adjusted year), and electrophysiologic testing ($12,300/quality-adjusted year). Because electrophysiologic testing has a lower marginal cost/effectiveness ratio than empiric drugs, one should be willing to perform electrophysiologic testing if one were willing to give empiric drug therapy and if one had sufficient resources, because society would receive more effectiveness for each dollar spent. Thus, it makes sense to compare electrophysiologic testing with observation. The marginal cost is $23,830 and the marginal effectiveness is 18 quality-adjusted months. Thus, the cost/effectiveness ratio is $15,900/quality-adjusted year. These relations are displayed in the graphic representations of Figure 3.

Sensitivity analyses. We examined the effect of changes in the assumptions of the analysis on the results. We illustrate these sensitivity analyses by demonstrating the effect of two probabilities—the likelihood of bradyarrhythymia and the likelihood of ventricular tachyarrhythmia—which, in any given patient, are likely the "softest" data in the analysis. Figure 4 shows the results in a patient with normal left ventricular function; in that case, bradyarrhythmia is the most likely etiology. Figure 5 shows the results in a patient with impaired left ventricular function; in that case, ventricular tachyarrhythmia is the most likely etiology. In both analyses, the probabilities of the other diagnoses are varied proportionately.

In the patient with normal left ventricular function (Fig. 4), expected survival increases for any strategy that includes pacing (that is, empiric pacing, empiric dual therapy and electrophysiologic testing) because the probability of ventricular tachyarrhythmia (the most life-threatening etiology) declines as the probability of bradyarrhythmia increases. For probabilities of bradyarrhythmia greater than 38%, empiric pacing offers the greatest quality-adjusted survival; for probabilities less than 38%, electrophysiologic testing offers the greatest quality-adjusted survival. This crossover point is called the threshold probability. In the patient with depressed left ventricular function (Fig. 5), expected survival declines for all strategies except electrophysiologic testing as the probability of ventricular tachyarrhythmia increases. The expected survival with electrophysiologic testing increases because appropriate drug therapy can be given. In this case, the threshold probability of ventricular tachyarrhythmias is 10%; for probabilities below that value, empiric pacing offers the highest quality-adjusted survival; for probabilities above that threshold, electrophysiologic testing is the best strategy in terms of survival.

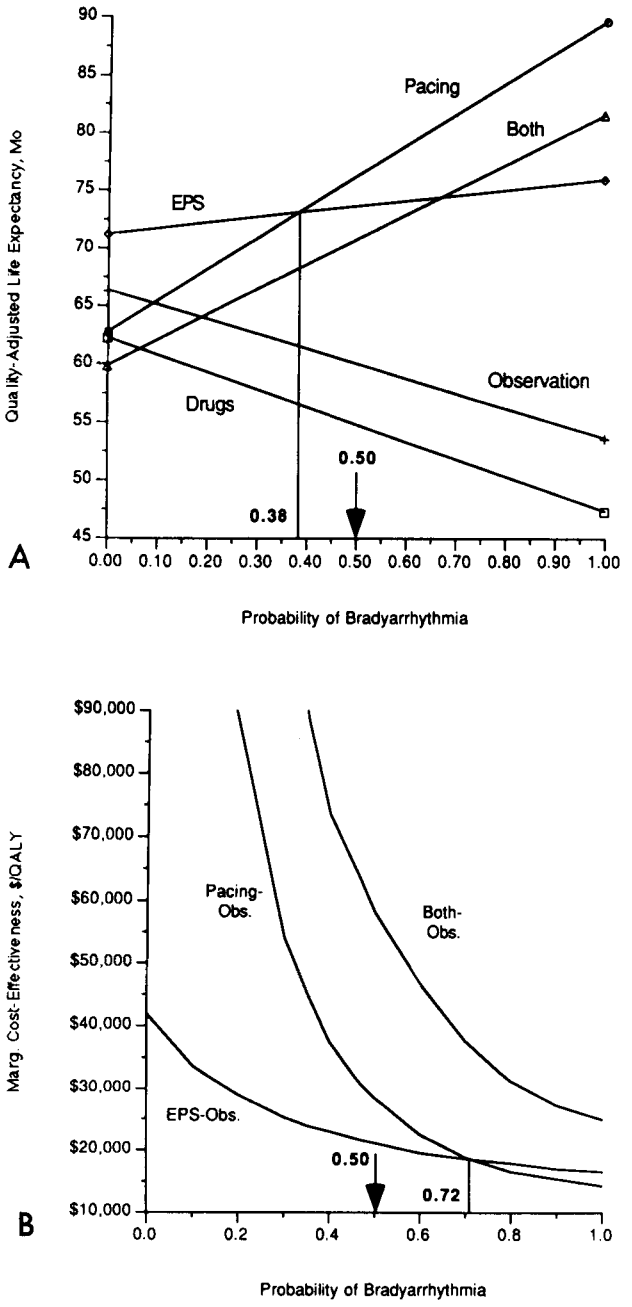

Figure 4. One-way sensitivity analyses in the patient with normal left ventricular function. The **horizontal axes** represent the probability of bradyarrhythmic etiology of syncope. The **vertical lines** illustrate the threshold probabilities; the **arrows** represent baseline conditions. **A, Vertical axis** represents the quality-adjusted life expectancy. **B, Vertical axis** represents marginal (Marg.) cost-effectiveness of different strategies. **Lines** represent comparisons between invasive strategies and observation. Abbreviations as in Figure 1; QALY = quality-adjusted life-year.

The marginal cost-effectiveness will be affected by the probability of bradyarrhythmia or ventricular tachyarrhyth-

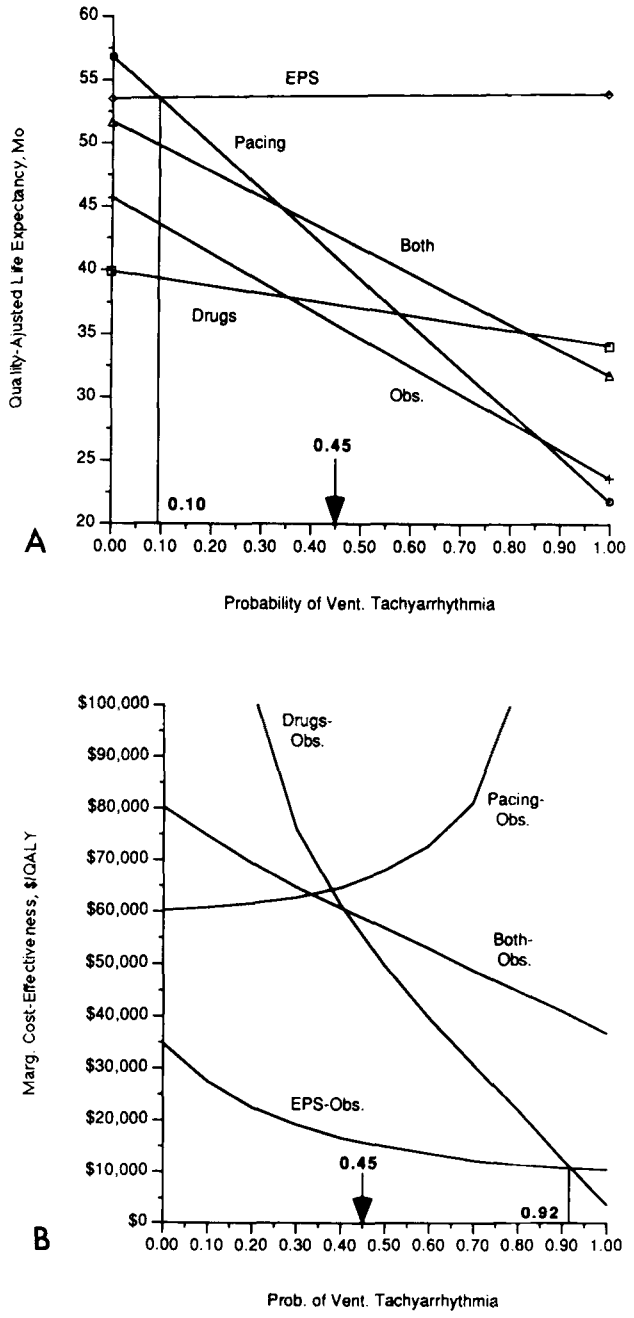

Figure 5. One-way sensitivity analyses in the patient with poor left ventricular (Vent.) function. The **horizontal axes** represent the probability of tachyarrhythmic origin of syncope. Format as in Figure 4. Abbreviations as in Figures 1 and 4.

mia (Fig. 4 and 5). In the case of normal left ventricular function (Fig. 4), electrophysiologic testing is the most cost-effective strategy if the probability of bradyarrhythmia is below 72%. Above the threshold, empiric pacing is most cost-effective. Note that the strategy of empiric dual therapy is always less cost-effective that either electrophysiologic testing or empiric pacing. If the probability of bradyarrhythmia is below 38%, electrophysiologic testing is both most effective and most cost-effective; if the probability is between 38 and 72%, than pacing is most effective but electrophysiologic testing is most cost-effective; if the probability is above 72%, then empiric pacing is both most effective and most cost-effective. The situation is different in the case of impaired left ventricular function (Fig. 5). Electrophysiologic testing is most cost-effective until the probability of ventricular tachyarrhythmias exceeds 92%; beyond that value, empiric drug therapy is most cost-effective but not the most effective. Below a probability of 10%, empiric pacing is most effective but electrophysiologic testing remains most cost-effective.

Another analysis of particular interest is the effect of simultaneous change in both the likelihood of ventricular tachyarrhythmias and the probability of bradyarrhythmic conduction defects (Fig. 6). In terms of quality-adjusted expected survival, observation is the best option at low probabilities of bradyarrhythmic conduction disturbance and ventricular tachyarrhythmia (that is, near the origin, where the most likely etiology is nonarrhythmic syncope). At relatively high likelihoods of bradyarrhythmic disease and low likelihoods of ventricular lesions, empiric pacemaker therapy is most effective (but not necessarily cost-effective, see earlier). At higher likelihoods of ventricular disease and lower chances of bradyarrhythmic syncope, electrophysiologic testing offers the greater expected survival.

The effects of age and co-morbidity (or load) on the expected survival and quality of life were studied in several Markov analyses. In virtually all cases the absolute survival decreased for all strategies proportionately. Inasmuch as costs tend to be high at the outset (that is, hospitalization and initial pacing), cost-effectiveness varies directly with age and co-morbidity.

Discussion

Cardiac pacemakers are associated with few medical risks and provide prolonged life expectancy and improved quality of life for many patients with symptomatic bradyarrhythmias. Nevertheless, a great deal of attention has been focused on widespread use of this technology, in part because it is considered expensive and in part because sharply defined indications were slow to be established. Guidelines issued by the Health Care Financing Administration (57) promote the general policy of reimbursing pacemaker implantations only when a clear relation between bradycardia and symptoms has been established. This requirement has led some clinicians to recommend invasive electrophysiologic studies to establish such a relation. Although such testing is relatively low risk (much like the empiric use of pacemakers), it too is quite expensive. Thus, one must ask whether such testing protocols are a cost-effective use of the nation's resources or whether other strategies should be considered.

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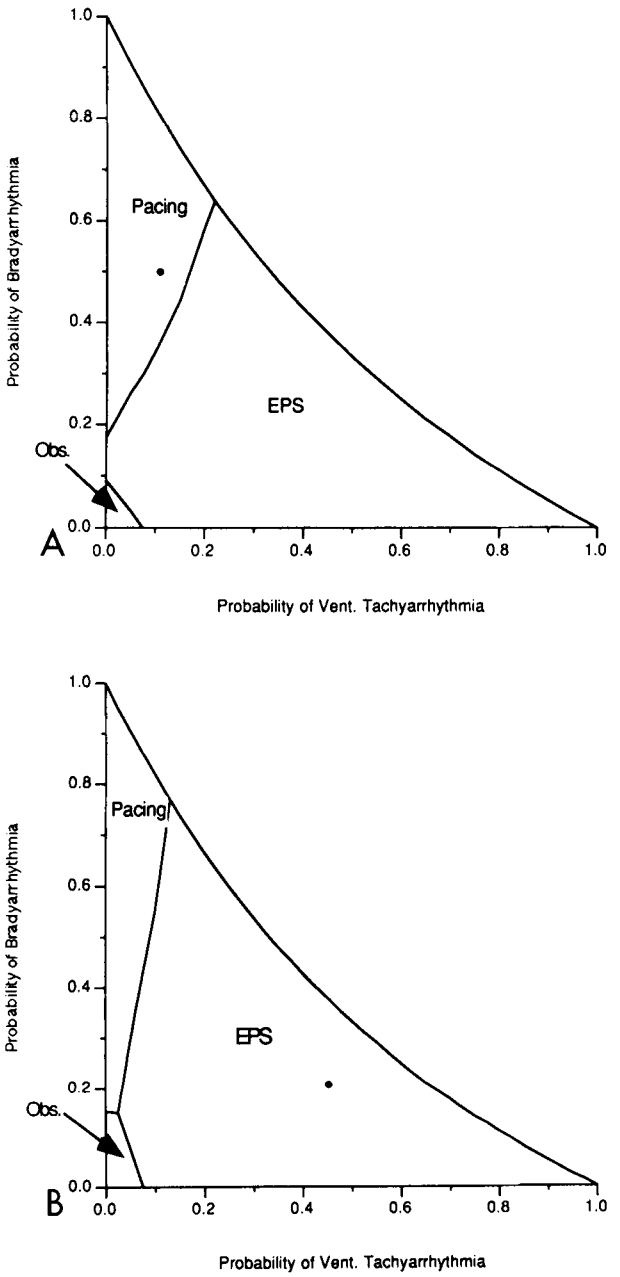

Figure 6. Two-way sensitivity analyses of the probabilities of bradyarrhythmia and ventricular (Vent.) tachyarrhythmia. Each point inside the **curved triangle** defines a unique combination of these probabilities; the region in which the point lies defines the most effective strategy, in terms of quality-adjusted life expectancy. The **black dot** on each figure represents baseline conditions. **A** and **B** represent a patient with normal and poor left ventricular function, respectively.

Modeling Issues

This review demonstrates how decision analysis, cost-effectiveness analysis and Markov modeling techniques can be used to approach vexing questions in cardiology. Several basic principles underlie these analytic techniques. First and foremost, such models are explicit. Each assumption is listed and quantitated—not to provide greater accuracy—but to allow the physician, the policy analyst and even the patient to understand the reasoning that lies behind these conclusions.

Decision analyses. A standard decision analysis involves five basic steps. 1) A model is constructed that represents a well focused question in sufficient detail to provide reasonable insights. 2) The probability of each potential diagnostic and therapeutic outcome is assessed, from objective data (when they are available in the published reports or in clinical data bases) or from the subjective opinions of experts. 3) The various potential outcomes are delineated and assigned relative value on a consistent scale. Often, such scales involve consideration of both the quantity and quality of life. 4) The expected value of each therapeutic strategy is calculated using two basic rules: when a choice can be made, pick the better option; when a chance is faced, assign an expected value based on the weighted average of the values of the potential outcomes, where the weighting factors are the likelihoods of the outcomes' occurring. 5) Finally, extensive sensitivity analyses are performed to determine how the conclusions of the analysis would be changed if the assumptions were different but still plausible.

Estimation of diagnosis and prognosis. In this analysis, two further modeling complexities were added. Our model combines a decision tree, to represent the diagnostic possibilities and the results of electrophysiologic testing, and a Markov or state transition model to estimate prognosis. In a Markov process model, the analyst specifies a limited set of states of health, an incremental utility for each state and a set of transition probabilities that govern the flow of patients from one state to another. A cohort stimulation then follows a population of patients as they move from one state to another, until all members of the simulated cohort "die." The expected value assigned to such a cohort's prognosis is then the sum of the products of each incremental utility times the number of patients in each state. Such models simply represent a compact formulation of extremely deep decision trees. Our model involved only four states of health. If we used a classic decision tree representation, the tree would have contained several thousand nodes and would have required four or five journal pages to represent. Trees of such complexity would provide the clinician with little insight and would be subject to many hidden errors.

Cost-effectiveness analysis. Second, we performed a cost-effectiveness analysis so we were actually using two separate value scales (dollars and quality-adjusted life-years), rather than combining them into a single scale. Cost-effectiveness analysis can identify some strategies that are inferior in terms of both cost and effectiveness (for example, the empiric use of drugs and pacing in a patient with symptomatic bifascicular block and normal left ventricular function). Such strategies are said to be "dominated." When such strategies are removed from consideration, one is left

with an array of options that can be ordered to provide increasing effectiveness (for example, survival) at increasing cost. There are no absolute guidelines about how much is too much to spend to gain an additional unit of effectiveness, that is, an additional year of survival. By comparing the analytic result to similar analyses of both a commonly accepted therapy (such as coronary artery surgery) and a therapy acknowledged to be very expensive (such as transplantation), the physician and analyst can garner a framework for comparison.

Complexity of the analytic model: role of computer support. Decision analytic models are constructed not to provide a single answer but to provide insights into a problem and must be explored under a variety of assumptions. If such models are of substantial complexity (as is the case here), their design, analysis, debugging and interpretation can involve a significant computational burden. The analysts' ability to construct and use such models then becomes limited by the feasibility of performing such calculations. Computational support is available in three main ways. First, special computer programs can be written to analyze a specific model (58,59). Second, general decision tree analysis software can be used (60–63). Third, general productivity software such as spreadsheets can be used. In fact, spreadsheet programs can be particularly useful in creating Markov models.

Clinical Issues

Empiric pacemaker therapy versus electrophysiologic testing in patients with normal left ventricular function. The relative benefit of electrophysiologic testing must depend on the likelihood that a pacemaker-responsive etiology of the patient's symptoms is, in fact, present and on the likelihood that electrophysiologic testing will identify another treatable cause. In this analysis, we examined the question of empiric pacemaker therapy versus electrophysiologic testing in symptomatic patients with bifascicular block in whom noninvasive evaluation has been unrevealing. Because these patients have a higher probability of pacemaker-responsive syncope than do most patients with syncope, we expected empiric pacing to be a reasonable strategy. Our analytic results were quite surprising, however. Even in patients with normal left ventricular function (in whom the likelihood of a bradycardia was assumed to be 50%), electrophysiologic testing was more cost-effective than empiric pacing; the latter strategy would provide a very small additional survival compared with electrophysiologic testing (about 2.5 quality-adjusted months) but would cost, on average, an additional $5,700 because some patients who do not need a pacemaker would receive one. Thus, society could prolong such a patient's survival, but at the exorbitant cost of $68,000 for each life-year gained. In comparison, the strategy of performing electrophysiologic testing in such patients, compared with conservative management, would cost only $21,000 per quality-adjusted life-year gained. The latter costs are very much in line with other accepted therapies: $20,000/quality-adjusted year for coronary bypass in patients with moderate to severe angina (17) and $15,000/quality-adjusted year for antihypertensive therapy in moderately hypertensive patients (16). Electrophysiologic testing is usually limited to a few major tertiary centers. If electrophysiologic testing is not available for a given patient, one should compare the cost-effectiveness of empiric pacing with that of observation alone: empiric pacing provides improved survival (over 16 quality-adjusted months) at a cost of $28,000/quality-adjusted year.

Electrophysiologic testing versus empiric pacing in the patient with impaired left ventricular function. The situation is quite different in the patient with impaired left ventricular function in whom electrophysiologic testing provides substantially more survival (17 quality-adjusted months) compared with empiric pacing. Here, not only is electrophysiologic testing the most cost-effective strategy, but substantial effort should be made to seek electrophysiologic testing if it is not available locally. If empiric pacing is performed, the marginal cost would be $60,000 per additional year of life gained. It would, in fact, be more cost-effective ($31,000/quality-adjusted year) to use empiric drug therapy in these patients because the likelihood of ventricular tachyarrhythmia is substantially higher than in patients with normal left ventricular function (45 versus 10%).

Role of sinus node dysfunction. Because roughly 15% of patients with symptomatic bifascicular block have sinus node dysfunction and will experience improved quality of life (but no increase in overall survival) with pacemaker therapy, empiric pacing will provide a slightly greater quality-adjusted survival than our baseline estimate; quality-adjusted survival will be approximately 6 months longer, making the marginal cost-effectiveness of empiric pacing compared to electrophysiologic testing only $20,000/quality-adjusted year, a more acceptable allocation of resources.

What if pacing were less expensive? Although the lifetime costs of empiric pacing may seem high ($42,000 in a 65 year old man with normal left ventricular function), they were based on the actual billing records in a teaching hospital. Approximately 35% of these costs were ascribed to initial implantation, approximately 20% were ascribed to monitoring costs and fully 45% of these costs were ascribed to subsequent battery replacements. If the costs of implantation and replacement could be lowered (by using less expensive hardware, decreasing the hospital length of stay or increasing the average time between replacements), then the costs of both empiric pacing and electrophysiologic testing would decline, but a proportionately greater decline would be seen in the empiric pacing strategy. Nevertheless, electrophysiologic testing is always more cost-effective than is empiric pacing, although the empiric strategy will "buy"

additional survival in the patient with normal left ventricular function. If the cost of pacemaker implantation and battery changes can be decreased by 6%, then empiric pacing provides additional survival at a cost of $65,000/quality-adjusted year; if costs decrease by 13%, then additional survival is available at $53,000/quality-adjusted year; if costs drop by 20%, then additional survival is available at $17,000/quality-adjusted year, a value very much in line with accepted therapies. Thus, the strategy of aggressive empiric pacing should become more and more socially acceptable as the cost of pacing decreases.

Implications for health policy. The analysis reported here provides several important insights for clinicians and for individuals who determine health policy. First, there are some circumstances in which empiric pacing would be both more effective, and even more cost-effective, than electrophysiologic testing. In patients with normal left ventricular function, empiric pacing provides longer survival if the probability of bradyarrhythmia exceeds 38% (Fig. 4a) but is not more cost-effective than electrophysiologic testing until that probability exceeds 72% (Fig. 4b). Second, because the majority of the costs of pacing can be ascribed to follow-up and battery replacement, the lifetime costs will be even higher in younger patients who will incur these costs for a much longer period. This effect can be seen in Table 7, where the costs of empiric pacing are far higher in the patient with normal left ventricular function who will experience twice the survival time of patients with depressed ventricular function. Finally, comparing Figures 6A and 6B, we can see that the circumstances in which empiric pacing would provide enhanced survival are not very different in the setting of normal and depressed left ventricular function. Rather, the major difference between these two circumstances is the likelihood of ventricular arrhythmia, a diagnosis more than four times as likely in the setting of depressed left ventricular function.

Conclusions. From the standpoint of national policy about cardiac pacemakers, the most important effect of a decision analytic model should be neither blind acceptance nor adherence to its conclusions. Rather, we present this model to provoke active yet focused discussion of these issues, not solely on the basis of the conclusions of experts but also on the basis of the "facts"—both objective and subjective—that underlie such opinions. Although the model presented here focused on a narrow spectrum of patients (those with symptomatic bifascicular block), its basic structure is relevant to a far broader spectrum of clinical questions about the indications for cardiac pacing. Such a model could be readily adapted to other settings in which there is disagreement about the need for pacing. Certainly, there may well be settings in which pacing is overutilized, but the debate about its indications should be based on clearly defined assumptions and logic, not just on opinion and anecdotal reports. Because absolute certainty is rare in the practice of medicine, both the clinician and the policy analyst must recognize that firm documentation of the relation between symptoms and arrhythmias cannot always be established. An overly rigid requirement for diagnostic certainty may deprive some patients of important therapeutic benefits and may occasionally engender greater expense.

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